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Gynecological Factors Related to Anterior Cruciate Ligament Injuries in Women

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GYNECOLOGICAL FACTORS RELATED TO ANTERIOR CRUCIATE LIGAMENT INJURIES IN WOMEN

by

Melissa Tuominen
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An Independent Study

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Department of Physical Therapy

School of Medicine

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in partial fulfillment of the requirements

for the degree of

Master of Physical Therapy

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This Independent Study, submitted by Melissa Tuominen in partial fulfillment of the requirements for the Degree of Master of Physical Therapy from the University of North Dakota, has been read by the Faculty Preceptor, Advisor, and Chairperson of Physical Therapy under whom the work has been done and is hereby approved.

(Faculty Preceptor)

(Graduate School Advisor)

(Chairperson, Physical Therapy)

PERMISSION

Title Gynecological Factors Related to Anterior Cruciate Ligaments in Women

Department Physical Therapy

Degree Master of Physical Therapy

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Signature Melissa Joaquin

Date 12/15/97

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I would like to thank Dr. Mark Lundeen for his support and guidance throughout my life, and for assisting me in my research. I would also like to thank Bev Johnson for letting me take one of her ideas and run with it. Most of all I would like to thank my family, especially my parents. Without them I would have never been able to make my dreams a reality. And finally, thank you Jason, for always making me smile.

ABSTRACT

Current literature has just begun to look at gynecology and obstetrics beyond the point of pregnancy and into the realm of sports medicine. Clinical research is starting to determine that female athletes may be predisposed to musculosketal injuries because of regular hormonal fluctuations. The purpose of this study is to determine whether there is a correlation between ACL injuries in females and a specific phase of their menstrual cycle. Survey's were mailed to 52 female patients who had undergone ACL reconstructive surgery within the past year. Twenty-five (48%) of the women completed and mailed back the survey. A majority of the respondents (64%) reported being injured during the proliferative and first half of the luteal phases of their menstrual cycle, the point in the cycle where estrogen and progesterone concentration is greatest. Further research is needed to determine the effect of hormone levels on injury rate.

CHAPTER I

INTRODUCTION

"No person in the United States shall, on the basis of sex, be excluded from participation in, be denied the benefits of, or be subject to discrimination under any educational program of action receiving federal financial assistance."[1] These are the words from the Title IX rule, which helped to initiate equality among men and women in athletics. A greater number of women have become athletic since the passing of this law, and the popularity of women's sports is steadily increasing. Women have proven that they are capable to compete equally to men, but with an increase in participation comes an increase in injuries.

One particular injury that is commonly seen in women is injury to the anterior cruciate ligament (ACL). In 1985 the staff of the British Columbia Sports Medicine Clinic noticed a trend toward increasing frequency of referrals of female basketball players with knee injuries.[2] They undertook a project to determine the incidence of ACL injuries in female basketball players referred to their clinic. Of 76 women studied over a period of 30 months, 55 injuries involved the knee, and 19 of these were ACL ruptures. ACL ruptures constituted 25% of all female basketball injuries seen at the clinic with only four male basketball players (out of 151) sustaining ACL ruptures during the same time period.

Zelisko et al[3] studied professional basketball players during two consecutive seasons. Results indicated women's overall injury frequency was 1.6 times that of men.

Knee injuries constituted 16% of women's injuries and only 12% of men's injuries. Many other studies[4,5,6,7,8,9,10] have indicated similar results.

Various factors have been studied that may increase the risk of injuries to female ACL's as compared to men[11,12,13]. Some of these factors include differences in strength, conditioning, differences in lower extremity alignment, intercondylar notch size, ligament laxity and possibly hormonal changes that occur within the body.

In contrast to men, women go through an endocrine cycle every month. Studies suggest that the fluctuating hormone levels can have an effect on injury rate. Liu et al[14,15] hypothesized that female steroid hormones may have an effect, directly or indirectly, on the structure of the anterior cruciate ligament. Moller-Neilson et al[16] studied 108 female soccer players to determine if injuries correlate with specific phases of the menstrual cycle. They recorded increases in injury rates both premenstrually and menstrually among women with moderate to severe premenstrual symptoms. The authors of this and other studies indicate a need for more research on how changes in hormone levels affect the incidence of injuries.[14,15,17,18,19]

The purpose of this study is to determine, retrospectively, if changes in hormone levels during the menstrual cycle affect one particular sport-induced trauma, ACL ruptures. This information can be used to enhance the knowledge of women and the health care professionals working with them, in order to prevent severe ligamentous injuries.

CHAPTER II

LITERATURE REVIEW

It has been well documented that female athletes have a significantly higher prevalence of anterior cruciate ligament (ACL) injuries than do male athletes;[2,3,4,5,6,7,8,9,10] although, the etiology remains unknown. Possible explanations involving gender related differences include lower extremity alignment, strength, conditioning, ligament laxity, and hormonal influences. "An area that has received very little study is the role of hormonal differences in predisposing female athletes to injury of the anterior cruciate ligament."[14]

Knowledge of anatomy is a prerequisite for any discussion about injury to the ACL.[20] Ligaments are short bands of fibrous tissue which bind bone to bone and provide support to joints as well as internal organs.[21,22] They are relatively inelastic and function to limit and guide joint motion.[22] The anterior cruciate ligament is composed of two principle portions, the anteromedial and posterolateral bands. The fascicles of the anteromedial band originate at the proximal aspect of the femur and insert on the anteromedial portion of the tibia. The fascicles of the posterolateral band originate at the proximal aspect of the femur and insert on the posterolateral portion of the tibia.[20]

Because of its structural orientation, the ACL remains taut throughout the entire knee range of motion, with lesser tension present from 30 to 60 degrees.[23] During knee extension the posterolateral band becomes taut, while during knee flexion the anteromedial portion becomes taut.[20,24] In general, the ACL prevents anterior

displacement of the tibia on the femur and limits internal and external rotation of the tibia on the femur.[25]

Ligaments are described as dense, regular connective tissue.[21] Structurally, about 90% of the ACL is composed of well-aligned collagen fibers, with approximately 10% of the structure consisting of elastic fibers.[26] Histological assessment of the ACL demonstrates longitudinally orientated bundles of collagen with fibroblasts located on either side of these bundles. Approximately 20% of the total tissue is fibroblastic and 80% of the structure consists of extracellular matrix. The extracellular matrix is made up of water (70%) and solid material (30%). The solid material consists of collagen, ground substance, and small amounts of elastin. Collagen molecules are formed into a triple-helix, with hydrogen bonded cross-links providing stability to the molecule by giving strength to the tissue and increasing the tolerance to mechanical stress. The elastin within ligaments provides for some elasticity or extensibility. The ground substance in ligaments consists primarily of proteoglycans, which function to bind the extracellular water in the matrix and act as a glue to stabilize the collagen fibers and enhance the strength of ligaments.[22]

Liu et al[14] identified estrogen and progesterone receptors in the nuclei of synoviocytes, stromal fibroblasts, and cells in the walls of the blood vessels of the anterior cruciate ligament. A total of 17 ACL specimens were collected, eleven were obtained from total knee replacements secondary to osteoarthritis, three from reconstruction of the ACL, two from medial meniscectomies, and one from an amputation secondary to chondrosarcoma of the hip. The ligament specimens were tested to see if they contained both estrogen and progesterone binding sites. Fourteen specimens exhibited marked staining for both the estrogen and progesterone receptors. Those that did not exhibit clear staining for estrogen receptors were from women ages 67, 73 and 74. Those that did not show clear staining for progesterone receptors were from a

47 year old male and two women 73 and 75 years old. The localization of the estrogen and progesterone receptors suggest that female steroid hormones may have an effect on the structure of the ACL.

Collagen has been studied under the influence of estrogen by three different groups of researchers. Fischer[18] studied the effect of estradiol on collagen of fascia and tendon in rats. They found that estrogen decreases the synthesis of collagen in tendon and causes increased degradation of collagen in fascia. Dyer et al[19] studied the effect of a single dose of estradiol on collagen metabolism in the uterus and various oral tissues in rats. Total collagen content of the uterus was not significantly altered, suggesting both synthesis and degradation of collagen. In rat oral tissue, there was a decrease in newly synthesized collagen in the molar periodontal ligament. Liu et al[15] investigated the effects of estrogen on the cellular proliferation and collagen synthesis of fibroblasts derived from rabbit anterior cruciate ligaments. Collagen synthesis as well as fibroblast proliferation was significantly reduced with increasing concentrations of estrogen. "Clinically, alterations in anterior cruciate ligament cellular metabolism caused by estrogen fluctuations may change the composition of the ligament, rendering it more susceptible to injury."[15]

A review of the menstrual cycle is necessary to determine at what point in the menstrual cycle women display increased levels of estrogen. The menstrual cycle is divided into five separate phases: menstrual, follicular, proliferative, ovulatory and luteal. The average length of the menstrual cycle is 28 days, however the length can be quite variable. The mean is between 25 and 30 days.[27,28]

Each phase is separated according to the events that take place. The menstrual phase begins on the first day of menses. Estrogen and progesterone are at low levels, which stimulate the hypothalamus and pituitary to secrete lutenizing hormone(LH) and follicular stimulating hormone(FSH). These hormones stimulate the ovaries to begin a

new reproductive cycle, by FSH stimulating the development of the follicle within the ovary and LH increasing estrogen production within the ovaries. This phase usually last approximately five days.[28,29]

The next phase, the follicular phase, is marked by the steady increase in estrogen and LH production. The rising estrogen creates a negative feedback loop on the pituitary, signaling it to cut production of FSH. The rising estrogen also prompts the pituitary to secrete LH. The follicular phase is approximately six days in length.[27,28]

On days 12-13 of the menstrual cycle the female is in the proliferative phase. Estrogen production initially surges, which means that LH is also surging. The production of estrogen then drops off causing FSH production to begin again.[27,28]

Day 14 is considered to be ovulation in the normal menstrual cycle. This is when the egg is released from the ovary, and the corpus luteum begins to produce progesterone. The purpose of progesterone is to prepare the uterine lining for pregnancy.[27,28]

During the second half of the cycle, progesterone continues to rise. This phase is considered to be the luteal phase and extends from day 15 through the end of the cycle, or day 27. By day 22, if pregnancy does not occur the corpus luteum will begin to shrink and stop producing progesterone. LH, FSH, progesterone and estrogen are at their lowest levels, by day 27. This is when menstruation will begin again. Figure 1 summarizes the changes in estrogen levels throughout the normal menstrual cycle.[27,29]

Large amounts of research has been completed on the effect of the menstrual cycle on physical performance, but is beyond the scope of this study. However, existing research on the effect the menstrual cycle may have on the incidence of musculoskeletal injuries to women is quite scarce.

Moller-Nielson et al[16] studied 108 female soccer players in Sweden. Women were initially asked to fill out a questionnaire concerning menstrual history,

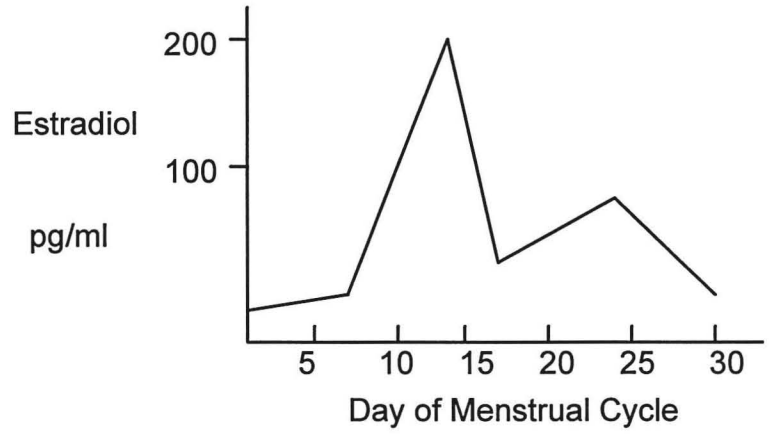

Fig.1-Estrogen Level Changes During the Normal Menstrual Cycle

contraception methods, and menstrual disorders. The women then noted their menstrual periods over a 12-month time period. All traumatic injuries which prevented the player from attending at least one practice or game, were recorded by both the coach and the player. Accurate records were kept by eighty percent of the 108 subjects and were analyzed by the researchers. This group of athletes were then divided into participants using oral contraceptives (OC) and participants not using OC's. Six hundred and twelve contraceptively controlled cycles and 396 non-contraceptive cycles were studied.

When analyzing the entire population without regard to contraceptive status, there was an increase in injury rate during the premenstrual and menstrual period ($p<.05$). Also groups who reported moderate to severe premenstrual symptoms had a higher premenstrual injury rate, whereas, the athletes with no complaints of premenstrual symptoms had a lower incidence of injury. There was no significance in injury rate during any phase of the menstrual cycle when the oral contraception users were analyzed.[16]

The same researchers completed a literature review on the relationship of oral contraceptive (OC) use and sports injuries a few years later[17]. The conclusions include the following: 1) OC users had better neuromuscular coordination (no study sited), 2) OC use reduced blood loss, thus maintaining higher hemoglobin levels, thus increased oxygen transport, and 3) the estrogen component of OC's has a beneficial effect on bone mineral content. They also hypothesized that OC use could have a detrimental effect because of the increase in joint laxity. This was not substantiated by any particular study.

It is interesting to note that many sources listed hormonal factors as being a possible predisposing factor for ACL injury, but only one source explains possible physiological mechanisms for this theory. Liu et al[14,15] hypothesized that acute fluctuations of estrogen concentration (i.e. during the menstrual cycle) may induce

changes in the metabolism, amount, type, and crosslinking of collagen in the ACL, thus predisposing female to injury.

CHAPTER III

METHODS

A list of fifty-two women were obtained from a local orthopedic surgeon. Each of these women had their torn anterior cruciate ligament reconstructed within that last year by this surgeon or by one of his partners. The age range of these women was from thirteen to thirty-eight. To eliminate the influence of menopause, women over the age of forty were excluded from the study.

Each subject was sent a survey and consent form (appendix A). The consent form contained a section for parent or guardian signature for subjects under the age of eighteen. Any survey returned without the consent form or consent forms that did not contain the proper signatures were excluded from the study.

The survey was constructed so that the episodic memory of the subject may be recalled. Each injury occurred as a result of some event or episode. By asking the subject to describe how her specific injury occurred, the complete episode could be recalled. Any significant problem, such as dealing with menstruation at the time of injury/surgery may also have been remembered. In addition to the details of how the ACL injury occurred, the subject was asked to complete a menstrual cycle history. This history included severity ratings of premenstrual symptoms, regularity of the subjects menstrual cycle, and a question asking at what point of the menstrual cycle the subject was in at the time of injury. To complete this final question, the menstrual cycle was broken down into four parts; 1) during menstruation (menstrual phase), 2) within the six days after menstruation (follicular phase), 3) within the six days before menstruation (end

of luteal phase), and 4) somewhere between these phases (proliferative, ovulation and first half of luteal phases).

Survey and consent forms were sent out on September 15, 1997. A follow-up reminder was sent out November 1, 1997 to the subjects that didn't return their survey. Any survey returned after November 15, 1997 was excluded from the study.

Data analysis was completed using the SPSS^{TM*} computer software. Statistical analysis was limited to descriptive statistics due to the limited number of subjects in each of the four injury groups (before, during, after and between).

Statistical Package for the Social Sciences, SPSS Inc., 444 North Michigan Ave., Chicago, IL 60611

CHAPTER IV

RESULTS

Fifty-two women were sent a survey and consent form. Of those, twenty-five (48%) returned both their survey and signed consent form. The respondents ranged from ages fourteen to thirty-seven with seventy-two percent of the women under the age of twenty-one. A majority of the respondents (72%) reported hurting themselves playing basketball. Other injuries occurred during volleyball (4%), skiing (4%), softball (4%), rodeo (4%), other (8%), and no response (4%).

Time since injury ranged from five months to eighty-nine months (7 1/2 years), with a median of fourteen months. Most of the respondents waited over one month (72%) before undergoing surgical repair of their anterior cruciate ligament.

Nineteen (76%) of the women reported having regular menstrual cycles at the time of injury. Regularity of menstrual cycles varied between subjects, but none of the women were amenorrheic or reported having a hysterectomy. Each of the respondents were asked to rate their premenstrual symptoms on a zero to three scale (0=no symptom, 1=mild, 2=moderate, and 3=severe). The following three symptoms were rated: abdominal cramps, breast swelling and irritability. Seven subjects (28%) reported having mild to no premenstrual symptoms (mean rate of symptoms ≤ 1.0); fourteen (56%) reported moderate symptoms (mean rate of symptoms >1.0 and <2.0); and four (16%) reported severe symptoms (mean rate of symptoms ≥ 2.0). Table 1 summarizes how each subject rated their premenstrual symptom.

Table 1.-Premenstrual Symptom Ratings Expressed In Percentage of Subjects

RATING	IRRITABILITY	BREAST SWELLING	ABDOMINAL CRAMPS
0	4	36	16
1	44	40	16
1.5			4
2	40	20	52
2.5	4		
3	8	4	12

When asked what phase of the menstrual cycle were the subjects in at the time of injury, sixteen (64%) responded that they were somewhere between cycles (between proliferative and first half of the luteal phases). Two (8%) stated that they were menstruating during injury (menstrual phase); three (12%) were injured just before menstruation (end of luteal phase); and three (12%) were injured just after menstruation (follicular phase). Figure 2 summarizes these results. Of the four respondents who had severe premenstrual symptoms, two (50%) were injured between, one (25%) was injured during, and one (25%) was injured after menstruation.

Age does not change the reported phase of injury. Of those subjects under the age of twenty-one (72%), eleven (64.7%) were injured between, two (11.8%) were injured during, three (17.6%) were injured before, and one (5.9%) was injured after menstruation.

Interferential statistics were not completed on the subjects because of the limited number of respondents and because there weren't at least six people in each of the four phase groups.

One unexpected result of the study was the many comments received from the subjects. Two subjects wrote personal letters explaining the difficulty they had dealing with their injury. One additional subject expressed her gratitude that someone was researching this topic. All of the subjects were interested in receiving the results of the study.

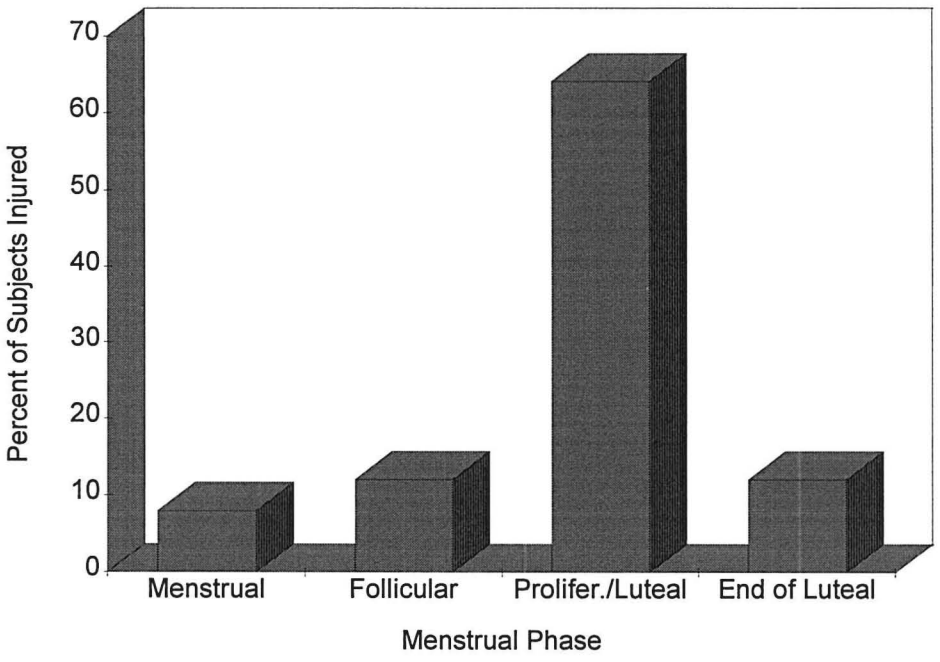

Figure 2.- Phase When Injury Occurred

CHAPTER V

DISCUSSION

In the normal menstrual cycle, estrogen and progesterone peak at approximately day 14 or during the first part of the luteal phase of the menstrual cycle. According to researchers[14,15,18,19] collagen synthesis is decreased and collagen degradation takes place in the presence of high levels of estrogen. Hypothetically, this would mean that women may be more susceptible to injuries sometime after day 14 of the menstrual cycle. It is unknown at this time whether the collagen degradation or decreased synthesis of collagen is immediate or delayed, so time of possible increased injury susceptibility is also unknown.

The results of the survey indicated a trend toward a higher injury rate in women during the proliferative and beginning of the luteal phases of the menstrual cycle (64%). This does not agree with Moller-Nielson et al[16], as they found a significantly increased injury rate just before and at the beginning of menstruation (end of luteal phase and beginning of menstrual phase) in women with severe premenstrual symptoms. Only four respondents in the current study had severe premenstrual symptoms, so a trend towards injury was not established.

An interesting result of the survey was that most of the respondents were under the age of 21 and most were injured playing basketball (72%). This would seem to indicate that younger women who play basketball are at a greater risk for ACL injuries. This agrees with Gray et al[2] as they found that 25% of the female basketball players seen

at their clinic had ruptured their ACL. Only 3% of their male counterparts had ACL injuries.

One unexpected result of the survey was the interest of the respondents. All who returned their survey indicated that they wanted to know the results, a few even wrote personal letters. One young woman wrote "I think this is great what you are doing. No one really takes what is happening to young athletes seriously." This young woman expressed feelings that no one really understands the severity of this injury and how it affects the athlete emotionally. For me, my whole self identity changed when I was injured. I believe that it would be beneficial to study the psychological changes that go along with this type of injury. Many young athletes aren't getting the emotional support they need.

There were several limitations to this study. The fact that the survey was completed retrospectively, was a major limitation. Subjects were chosen because they underwent surgery during the last year, in hopes that they may remember their menstrual cycle status at the time of injury. It was expected that most of the subjects had surgery within a couple weeks of their injury, but in fact only 28% underwent surgery within one month. Also, the median time since injury was fourteen months, with a range from five months to seven and one half years. The greater than anticipated length of time from injury to surgery may have affected the subjects ability to accurately recall during which phase of their menstrual cycle they were injured. The "safest" response would have been somewhere between. Therefore, the survey should be given to the subject during her first visit to the doctor, immediately after injury. This may improve the accuracy of memory about menstrual cycle status.

Another limitation was the small respondent size. Significance of results could not be computed because the sample size was less than thirty. Future studies should use

larger sample sizes to provide an opportunity to correlate injury to a specific phase of the menstrual cycle.

The effects of estrogen on muscles and ligaments need further study. Liu et al[15] indicated collagen degradation in the rabbit ACL, but no one has determined at which point in the menstrual cycle this is most likely to occur. Many researchers hypothesized that hormones play a role in injury to women, however the physiological mechanism was not explained. Also, the role of the hormone relaxin was not established in this study.

One other factor that needs to be determined is how the use of oral contraceptives may effect injury. Moller-Nielson et al[16] found an increase in injury rate among women with severe premenstrual symptoms, but this was decreased with women using oral contraceptives. Do oral contraceptives regulate the release of estrogen during the menstrual cycle, so that estrogen fluctuation is less severe? Would using oral contraceptives decrease women's susceptibility to musculoskeletal injury?

CONCLUSSION

It has been well documented that women have an increased prevalence of ACL injuries as compared to men. Many possible explanations exist, including hormonal factors, but research is limited in this area. Women are subject to regular hormonal changes each month that could have a possible effect on muscles, tendons and ligaments. Research needs to determine whether changes in hormone levels may predispose women to musculoskeletal injuries.

Results of this study show a trend towards increased ACL injuries during the first part of the luteal phase of the menstrual cycle, the point at which estrogen concentration is at its highest. This result may be due to the format of the questions in the survey or because the study was done retrospectively, so further research needs to be done prospectively to determine whether these results were accurate.

Clinically, health care professionals and women need to understand the effects hormones can have on them. To prevent musculoskeletal injuries in women, especially athletic women, appropriate strengthening and conditioning programs need to be instituted.

APPENDIX A

Melissa Tuominen

♦♦♦

2100 South 29th Street #121 ♦ Grand Forks, ND 58201
Home Phone 701-780-9345 ♦ Email mtuomine@prairie.nodak.edu

Hello, my name is Melissa Tuominen. I am a physical therapy student at the University of North Dakota, and I am conducting a study about knee injuries. I have torn both of my anterior cruciate ligaments (ACL's), and I want to look for possible ways to prevent these injuries in women. Because you have also experienced the same type of injury, I am inviting you to participate in my study. Your name was forwarded to me by Dr. Mark Lundeen of Orthopedic Associates.

The purpose of the study is to determine if there is a correlation between ACL injuries in females and a specific phase of their menstrual cycle. I hope to describe a predisposing factor unique to women that may increase their chance for musculoskeletal injuries. You are being asked to participate in this study because of your history of ACL injury and subsequent surgery.

You will be asked to fill out a short survey regarding the history of the injury to your knee and of your menstrual cycle. All you have to do is return the survey and this consent form in the envelope provided.

Your name will not be used in any reports of the results of this study. Any information that is obtained in connection with this study and that can be identified with you, will remain confidential and will be disclosed only with your permission. The data will be identified by a number known only by me. You are not obligated to participate in the study. Your decision whether or not to participate will not prejudice your future relationship with the Physical Therapy Department or the University of North Dakota. If you decide to participate, you are free to discontinue participation at any time without prejudice.

I will be available to answer any questions you have concerning the study. I can be reached at (701)780-9345 or you may direct your questions to my advisor, Bev Johnson, at (701)777-2831. A copy of this consent form is available to all participants in the study.

Results of the study will be used to educate health care professionals and their patients, so that further severe injuries can be prevented or at the very least minimized. If you would like a summary of the results please indicate so at the bottom of this consent form. The study will conclude on approximately December 1, 1997.

Your signature indicates that, having read the above information, you have decided to participate in the research project. If you are under the age of 18, your parent or guardian must also read and sign the consent form.

I have read all of the above and willingly agree to participate in this study explained to me by *Melissa Tuominen.*

_____
Participant's Signature Date

____ I would like to know the results of your study.

_____
Parent or Guardian Signature Date

Gynecological Factors Related to Anterior Cruciate Ligament Injuries in Women

Answer the following questions to the best of your knowledge. Return the survey and consent form in the enclosed envelope as soon as possible. Please remember to have parent or guardian sign consent form if you are under the age of 18. Thank you for taking the time to complete the survey and participating in my study.

Date of injury (mo/day/yr):_____ **Date of surgery** (mo/day/yr):_____.

Briefly explain how you injured your knee:

Date of birth (mo/day/yr):_____.

Please read the following table and rate each pre-menstrual symptom by putting a check mark under the number that applies to your menstrual cycle in general:

0=No symptom; 1=Mild symptom; 2=Moderate symptom; 3=Severe symptom

Symptom	0	1	2	3
Irritability				
Breast Swelling				
Abdominal Cramps				

At the time of injury what was the status of your menstrual cycle?

(please check the one that applies)

___Regular for greater than 3 months
___Irregular
___Absent for greater than 3 months
___Haven't begun menstruating or have had a hysterectomy

At what point of your menstrual cycle were you in when you were injured?**

(Please check the one that applies)

___During menstruation
___Right before menstruation (within 6 days before menstruating)
___Right after menstruation (within 6 days after menstruating)
___Somewhere between

**Menstruation refers to the time of the month when you are bleeding.

APPENDIX B

__EXPEDITED REVIEW REQUESTED UNDER ITEM__(NUMBER[S]) OF HHS REGULATIONS
__EXEMPT REVIEW REQUESTED UNDER ITEM__(NUMBER[S]) OF HHS REGULATIONS

UNIVERSITY OF NORTH DAKOTA
HUMAN SUBJECTS REVIEW FORM
FOR NEW PROJECTS OR PROCEDURAL REVISIONS TO APPROVED PROJECTS INVOLVING HUMAN SUBJECTS

PRINCIPAL INVESTIGATOR: Melissa Tuominen **TELEPHONE:** 701-232-6202 **DATE:** June 30, 1997

ADDRESS TO WHICH NOTICE OF APPROVAL SHOULD BE SENT: 3243 South 30th Ave, Fargo, ND 58103

SCHOOL/COLLEGE: School of Medicine **Department:** Physical Therapy **Proposed Project Dates:** 6/1/97-12/15/97

PROJECT TITLE: Gynecological Factors Related to Anterior Cruciate Ligament Injuries in Women

FUNDING AGENCIES (IF APPLICABLE): N/A

TYPE OF PROJECT:

X NEW PROJECT __CONTINUATION __RENEWAL __DISSERTATION OR THESIS RESEARCH

X STUDENT RESEARCH __CHANGE IN PROCEDURE FOR A PREVIOUSLY APPROVED PROJECT

DISSERTATION/THESIS ADVISOR, OR STUDENT ADVISOR: Bev Johnson

PROPOSED PROJECT: __Involves New Drugs __Involves Non-Approved Use of Drug

X Involves a Cooperating Institution

IF ANY OF YOUR SUBJECTS FALL IN ANY OF THE FOLLOWING CLASSIFICATIONS, PLEASE INDICATE THE CLASSIFICATION(S):

X Minors(< 18 Years) __Pregnant Women __Mentally Disabled __Fetuses __Mentally Retarded

__Prisoners __Abortuses __UND Students (>18 Years)

IF YOUR PROJECT INVOLVES ANY HUMAN TISSUE, BODY FLUIDS, PATHOLOGICAL SPECIMENS, DONATED ORGANS, FETAL MATERIAL, OR PLACENTAL MATERIALS, CHECK HERE _____.

1. ABSTRACT: (LIMIT TO 200 WORDS OR LESS AND INCLUDE JUSTIFICATION OR NECESSITY FOR USING HUMAN SUBJECTS.)

PLEASE NOTE: Only information pertinent to your request to utilize human subjects in your project or activity should be included on this form. Where appropriate attach sections from your proposal (if seeking outside funding).

Current literature has just begun to look at gynecology and obstetrics beyond the point of pregnancy and into the realm of sports medicine. Clinical research is starting to determine that women athletes may see increased injuries just before or during their menstrual cycle. The purpose of my study is to determine if there is a correlation between ACL injuries in females and a specific phase of their menstrual cycle. Survey's will be mailed to approximately 50 female patients who have undergone ACL reconstructive surgery within the past year, to determine whether a correlation with their menstrual cycle exists. It will be necessary to use human subjects to fill out this survey because pre-operative reports do not include information about menstrual cycle.

2. PROTOCOL: (Describe procedures to which humans will be subjected. Use additional pages if necessary.)

A list of approximately 50 females who have undergone ACL reconstructive surgery within the last year will be given to me by Dr. Mark Lundeen, an orthopedic surgeon with Orthopedic Associates of Fargo, North Dakota. See attached support letter. Each of these subjects will be mailed a survey regarding the injury to their ACL and a quick menstrual history (i.e.. severity of premenstrual symptoms.) Participants will be asked whether or not they can remember if they were menstruating during the time of injury or shortly after. Survey's will be sent to women who had their ACL reconstructed in hopes that being in a hospital may spark unique memories of having to deal with menstruation during surgery and the subsequent hospital stay. If the survey is not returned within one month a telephone call will be made to encourage participants to complete their survey and consent form. Surveys returned without completed consent forms will be dropped from the study. To ensure confidentiality, surveys and consent forms will be numbered. As soon as both are returned they will be separated and stored in different files. A list will be kept by me to ensure that all consent forms are properly filled out and returned. This list will only be seen by me and will be destroyed as soon as all consent forms are returned. Data will be analyzed using Pearson correlation statistics.

3. BENEFITS: (Describe the benefits to the individual or society)

Research to date has correlated hypermobility to the third trimester of pregnancy and most women understand that they might experience a greater risk for musculoskeletal injury. The hypermobility seen in many ligaments is attributed to circulating hormones. Circulating hormones also play a role during the menstrual cycle, thus possibly increasing risk for injury. This information could be used to enhance the knowledge of health care professionals working with women as they can educate clients to understand their unique propensity toward musculoskeletal injuries therefore, enhancing women's ability to prevent injuries. Participants will benefit by increasing their knowledge about possible reasons why their injury occurred and understanding how to prevent further injuries. Results of the study will also be shared with the physician's of the cooperating institution, students and faculty of the participating institution and if applicable published in a health care journal.

4. RISKS: (Describe the risks to the subject and precautions that will be taken to minimize them. The concept of risk goes beyond physical risk and includes risks to the subject's dignity and self-respect, as well as psycho-logical, emotional, or behavioral risk. If data are collected which could prove harmful or embarrassing to the subject if associated with him or her, then describe the methods to be used to insure the confidentiality of data obtained, including plans for final disposition or destruction, debriefing procedures, etc.)

No physical risk exist in the study. To insure confidentiality, surveys will not contain the name of the participant. Instead codes will be put on each survey and consent form. Consent forms will be separated from the surveys and the name of the patients will not be associated with the data. Psychological risks include a possible decrease in participant comfort level. Some of the questions are personal in nature. To increase comfort level, a short statement containing the purpose of the study and a statement about confidentiality will be included on the consent form.

5. CONSENT FORM: A copy of the **CONSENT FORM** to be signed by the subject (if applicable) and/or any statement to be read to the subject should be attached to this form. If no **CONSENT FORM** is to be used, document the procedures to be used to assure that infringement upon the subject's rights will not occur. Describe where signed consent forms will be kept and for what period of time.

Signed consent forms will be kept in a locked file cabinet in the Physical Therapy Department for a period of five years. A parents or guardian will be asked to sign each consent form for the participant if they are under the age of 18. A copy of the consent form is attached.

6. For **FULL IRB REVIEW** forward a signed original and thirteen (13) copies of this completed form, and where applicable, thirteen (13) copies of the proposed consent form, questionnaires, etc. and any supporting documentation to:

Office of Research & Program Development
University of North Dakota
Box 8138, University Station
Grand Forks, North Dakota 58202

On campus, mail to: Office of Research & Program Development, Box 134, or drop it off at Room 101 Twamley Hall.
For **EXEMPT** or **EXPEDITED REVIEW** forward a signed original and a copy of the consent form, questionnaires, etc. and any supporting documentation to one of the addresses above.

The policies and procedures on Use of Human Subjects of the University of North Dakota apply to all activities involving use of Human Subjects performed by personnel conducting such activities under the auspices of the University. No activities are to be initiated without prior review and approval as prescribed by the University's policies and procedures governing the use of human subjects.

SIGNATURES:

_____ **DATE:**
Principal Investigator

_____ **DATE:**
Project Director or Student Adviser

_____ **DATE:**
Training or Center Grant Director

REPORT OF ACTION: FULL BOARD REVIEW

University of North Dakota Institutional Review Board

DATE: July 29, 1997 **PROJECT NUMBER:** IRB-9707-017

NAME: Melissa Tuominen **DEPARTMENT/COLLEGE:** Physical Therapy

PROJECT TITLE: Gynecological Factors Related to Anterior Cruciate Ligament Injuries in Women

The above referenced project was reviewed by the Chair/Vice Chair/Designated Member of the University of North Dakota Institutional Review Board on July 30, 1997 and the following action was taken:

☒ Project **approved.** Next scheduled review is on July 1998.
(See REMARKS SECTION for any special condition.)

☐ Project approved **PENDING** receipt of corrections/additions in ORPD. These corrections/additions should be submitted to ORPD for review and approval. **This study may NOT be started UNTIL final IRB approval has been received.** (See REMARKS SECTION for further information.)

☐ Project approval **deferred. This study may not be started until final IRB approval has been received.** (See REMARKS SECTION for further information.)

☐ Project **denied.** (See REMARKS SECTION for further information.)

REMARKS: Any changes in protocol or adverse occurrences in the course of the research project must be reported immediately to the IRB Chairperson or ORPD.

cc: B. Johnson, Adviser
Dean, Medical School

Signature of Chairperson/Vice Chair/Designated Member
UND's Institutional Review Board

7/29/97
Date

If the proposed project (clinical medical) is to be part of a research activity funded by a Federal Agency, a special assurance statement or a completed 596 Form may be required. Contact ORPD to obtain the required documents.

(3/96)

THE GRADUATE SCHOOL
UNIVERSITY OF NORTH DAKOTA OUTLINE

(Check One)
Outline of Independent Study ___X___ Thesis _____ Dissertation _____ Project Design _____

Student: Melissa Tuominen Date: 10 / 22 / 97

Proposed Title: **Gynecological Factors Related To Anterior Cruciate Ligament Injuries In Women**

Anticipated Date of Graduation: 5 / 10 / 98

Description of the nature of the problem/study, the procedure or methodology to be followed, and the proposed results:

Current literature has just begun to look at gynecology and obstetrics beyond the point of pregnancy and into the realm of sports medicine. Clinical research is starting to determine that women athletes may see increased injuries just before or during their menstrual cycle. The purpose of my study is to determine if there is a correlation between ACL injuries in females and a specific phase of their menstrual cycle. The hypermobility seen in many ligaments during pregnancy is attributed to circulating hormones. Circulating hormones also play a role during the menstrual cycle, thus possibly increasing risk for injury.

A list of approximately 50 females who have undergone ACL reconstructive surgery within the last year will be given to me by an area orthopedic surgeon. Each of these subjects will be mailed a survey regarding the injury to their ACL and a quick menstrual history (i.e.. severity of premenstrual symptoms.) Participants will be asked whether or not they can remember if they were menstruating during the time of injury or shortly after. The results will be analyzed with the Pearson correlation coefficient to identify any significant correlation.

My hypothesis is that the data will show that a significant correlation exists between ACL injury and a certain phase of the menstrual cycle. If this is found to be true, further studies could be completed to determine the extent of hormone receptors located on tissues such as the ACL and how these collagen tissue are affected with different amounts of hormones present. The knowledge gained from this study could be used to enhance the knowledge of health care professionals, coaches and any person working with women, along with the entire female population to help prevent injuries.

Signatures of approval as specified in the "Degree Requirements" section of the Graduate Bulletin:

Beverly Jensen _____

DH 10-30-97

Red River Valley
Sports Medicine Institute

May 5, 1997

RE: MELISSA TUOMINEN

To Whom It May Concern:

Melissa Tuominen is an athlete who I have followed for many years. She has had experience with cruciate ligament reconstruction surgery and she approached me with a concept of evaluating the incidence of injury relative to female athletes' menstrual cycle. There really is not significant information in the literature correlating these two events in young female athletes' lives and I support the concept and am looking forward to her evaluation. In our office we will be most happy to give her information on at least 50 anterior cruciate injured athletes so as to allow her to do a retrospective review.

If you need any further information from me, please contact me at my office.

Sincerely Yours,

Mark A. Lundeen, M.D., P.C.

MAL/crb
Dict. 5-3-97

2301 25th Street South • Suite C
Fargo, North Dakota 58103
Tel 701-280-2406
Fax 701-237-0922

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